



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Merton Bernfield and Ofer Reizes  
Serial No.: 08/965,356                      Group Art Unit: 1632  
Filed: November 6, 1997                      Examiner: A. Baker  
For: METHODS AND REAGENTS FOR REGULATING OBESITY

Assistant Commissioner for Patents  
Washington, D.C. 20231

**DECLARATION UNDER 37 C.F.R. §1.132**

Sir:

I, Ofer Reizes, hereby declare that:

1. I am an inventor of the methods and compositions described and claimed in U.S. 08/965,356. I have read the Office Action mailed October 9, 1998, in this application.
2. The examiner has requested proof that the constructs described in the applications show preferential expression in the hypothalamus. Enclosed as Exhibit A are photographs showing syndecan-1 mRNA and proteoglycan derived from the transgene expressed in the anterior and posterior hypothalamic nuclei that regulate body weight. The Exhibit demonstrates unique expression of syndecan-1 in these transgenic mice to the hypothalamic

expression of syndecan-1 in these transgenic mice to the hypothalamic nuclei regulating energy balance, namely the arcuate, lateral, dorsomedial, supraoptic, and suprachiasmatic nuclei.

3. As shown in Exhibit B, fasting induces increased expression of syndecan-3 in hypothalamic extracts. Wild-type mice were fasted (3) or fed (3; controls). These were killed and their hypothalamus removed to examine for expression by Western blot of proteoglycans. The results demonstrate that syndecan-3 is upregulated when fasted.

4. It is important to point out that the functional part of the syndecans are their heparan sulfate chains. The core proteins are thought to be important for localization of the heparan sulfate to the cell surface or the extracellular milieu. Papers are attached as Exhibit C in support.

5. The CMV promoter/enhancer is not the only promoter that could be used to generate the claimed transgenic animals. Please see the attached nine abstracts (Exhibit D) describing the use of neuron specific enolase to generate transgenic mice. Additionally, the  $\beta$ -actin promoter has been used to generate mice overexpressing agouti and agouti-related protein (see Science 278, 135) and these mice become obese.

6. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements are made with the knowledge that willful false statements are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing

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thereon.

Date:

11/20/99

Ofer Reizes

A handwritten signature in cursive script, appearing to read "Ofer Reizes", written over a horizontal line.